

Notice of Allowability	Application No.	Applicant(s)
	08/405,454	SULLIVAN ET AL.
	Examiner	Art Unit
	CHERIE M. WOODWARD	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Response filed 3/21/2011 and Supplemental Response filed 6/30/2011.
2. ☒ The allowed claim(s) is/are 40-45,50,54-65, 67-71, and 73.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. <input type="checkbox"/> Notice of References Cited (PTO-892)	5. <input type="checkbox"/> Notice of Informal Patent Application
2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	6. <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date <u>20010707</u> .
3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>3/2/2011</u>	7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment
4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material	8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance
	9. <input type="checkbox"/> Other _____.
/CHERIE M WOODWARD/ Primary Examiner, Art Unit 1647	

EXAMINER'S AMENDMENT AND EXAMINER'S COMMENTS

1. Applicant's Response and Amendments filed 3/24/2011, 4/14/2011, 6/24/2011, and 6/30/2011 are acknowledged and entered. The Supplemental Amendments to the Claims, Drawings, and the Specification filed 6/30/2011 are ENTERED.
2. Claims 1-39, 43-49, 51-53, 66, 74, and 75 have been cancelled. Claims 40-42, 50, 54-65, and 67-73 are pending. Claims 40-42, 50, 56-65, and 67-73 have previously been under examination. Claims 54 and 55 are rejoined. Claims 40-42, 50, 54-65, and 67-73 are presently under examination.
3. The Information Disclosure Statement (IDS) filed 3/24/2011 is acknowledged and entered. A signed copy is attached.
4. Telephonic Interviews were held with Applicant's Representative Michael Siekman on 6/23/2011, 6/28/2011, and 7/28/2011. An Interview Summary is attached.
5. An Examiner's Amendment to the claims appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

6. Authorization for this Examiner's Amendment was given in a telephone interview with Applicant's representative Michael Siekman on 28 July 2011. Authorization was given to amend the claim language by Examiner's Amendment and pass the case to issue.

In the claims:

Cancel claim 72.

In claims 59 and 71 change all instances of "Fab₂" to "F(ab)₂".

7. Examiner's Comments:

During the two June 2011 Interviews, the First and Second Dart Declarations were discussed, as well as the First and Second Russell Declarations, the Sullivan Declaration, and the Smith Declaration. These Declarations were discussed and were found to be sufficient to remove the Sullivan (1984) reference as prior art.

On the issue of Written Description, the pharmacokinetics of the various fragments were discussed in terms of the venom depot effect. The examiner agrees that it is reasonable that the short half-life Fab fragments could rapidly reach venom toxins and neutralize them in an initial burst. Once the Fab fragments begin to clear, the larger F(ab)₂ fragments with a longer half-life would be available to bind any remaining venom toxins or venom toxins that would have moved out of, within, or around a tissue site due to the depot effect. Because of the difference in time-course effect and the different pharmacokinetic properties of the different fragments, in combination, they are able to provide a form of controlled release by which to better neutralize and clear venom toxins. Although there may be some overlapping competition for toxin binding it is reasonable, based on the evidence of record, that this competition would likely be minimized because of the differences in the various antibody fragment pharmacokinetics.

The combination of Fabs with F(ab)₂s and the discussion in the multiple Declarations of record (see above) regarding the venom depot effect (where venom may remain in tissues and leach out at a variable rate over time) provide sufficient reason for the Applicant's to have made a combinatorial Fab and F(ab)₂ preparation. This combinatorial reasoning was not known and/or

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not well understood in the art prior to Applicant's invention.

It is understood, based on the evidence of record, that there was a long-felt-need in the art at the time of the instant invention for an antibody fragment antivenom preparation that would be more effective in neutralizing venom toxins from snakes, given the clinical issues and the extant treatment methods available at the time of the invention, particularly due to the depot effect of envenomation.

Other issues related to Written Description were discussed in terms of the *Bothrops* genus and to the characterization of "more than one venom." Support for the venom of the species of *Bothrops atrox* is provided in the specification as part of the Wyeth ACP *Crotalidae* polyvalent antivenom (p. 17 of the specification). The ACP antivenom antibodies include antibodies against the venom of *Crotalus adamenus*, *Crotalus atrox*, *Crotalus durissus*, and *Bothrops atrox* species. The instant specification mentions and Sullivan and Russell (1983) reference discusses the Wyeth ACP antivenom preparation.

Obvious typographical errors in the specification and the drawings were also discussed and Applicant submitted corrections. Terminology related to antivenom versus antivenin were also discussed and it is accepted that these terms are used in the art interchangeably.

Claim 72 is being cancelled by Examiner's Amendment in light of the change in taxonomic nomenclature.

8. All of the rejections of record are withdrawn in light of Applicant's Arguments, Declarations, Amendments to the Claims, Specification, and the Drawings, and in light of the Examiner's Comments and Examiner's Amendment, as set forth above.

9. Claims 40-42, 50, 54-65, 67-71, and 73 are allowed with the aforementioned Examiner's Amendment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647